

## **Remarks**

### **Status of the Claims**

Claims 1-5, 7-11, 13-19, 22-25, 27-34, 36-44, 47-50, and 71-74 have been examined and are pending. Claims 59-70 have been previously withdrawn without prejudice in response to a Restriction Requirement set forth in the Office Action mailed March 20, 2006. After entry of this paper claims 1-5, 7-11, 13-19, 22-25, 27-34, 36-44, 47-50, and 71-74 remain pending for examination.

All claims stand rejected.

Claims 1-5, 7-11, 13-19, and 22 stand rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Levenberg et al. (PNAS, 99 (7): 4391-4396, 2002) (“Levenberg”).

Claims 1-5, 7-11, 13-19, 22-25, 27-34, 36-42, and 47-50 stand rejected under 35 U.S.C. § 103 as allegedly obvious over Levenberg in view of U.S. Published Application No. 2002/0146678 by Benvenisty et al. (“Benvenisty”).

Claims 1-5, 7-11, 13-19, 22-25, 27-34, 36-44, 47-50, and 71-74 stand rejected under 35 U.S.C. § 103 as allegedly obvious over Levenberg in view of Benvenisty and further in view of Kojima et al. (Experimental Cell Research, 206(2): 152-156, 1993)(“Kojima”)

### **Rejections under 35 U.S.C. §102 based on Levenberg**

Applicants must respectfully submit that Levenberg does not anticipate Applicants presently pending claims because Levenberg does not teach or mention a tissue engineering construct comprising smooth muscle cells having a three dimensional vascular network as set forth in Applicants’ claim 1. Rather, Levenberg speaks solely of endothelial cells and does not describe or teach one of ordinary skill in the art how to provide a tissue engineering construct comprising smooth muscle cells having a three dimensional vascular network. Absent a teaching of each and every element of Applicants’ claim 1, Levenberg cannot anticipate claim 1 or claims 2-5, 7-11, 13-19, and 22 that depend therefrom. Accordingly, Applicants’ submit that claims 1-5, 7-11, 13-19, and 22 are novel in view of Levenberg.

Rejections under 35 U.S.C. §103 based on Levenberg & Benvenisty

Applicants must respectfully submit that Levenberg and Benvenisty, either alone or in proper combination, do not render obvious Applicants presently pending claims because these references do not teach or fairly suggest a tissue engineering construct comprising smooth muscle cells having a three dimensional vascular network as set forth in Applicants' claim 1 or a method of making a tissue engineering construct comprising smooth muscle cells having a three dimensional vascular network as set forth in Applicants' claim 23.

As set forth above, Levenberg does not teach or even mention constructs comprising smooth muscle cells. In contrast, the present application does teach one of ordinary skill in the art embodiments of a tissue engineering construct comprising smooth muscle cells having a three dimensional vascular network and methods for making same (see, e.g., Specification at page 33).

Applicants submit that Benvenisty does not cure this deficiency in Levenberg because Benvenisty does not teach, alone or in combination with Levenberg, one of ordinary skill in the art how to provide a tissue engineering construct comprising smooth muscle cells having a three dimensional vascular network. Although Benvenisty does mention once in paragraph 0057 smooth-muscle cells this mention is the context of using cell cultures in place of animals for preclinical testing,

[0057] Additional uses for methods for providing cells that are differentiated partly or entirely along a particular cell lineage include in vitro uses such as creating reagents for drug toxicity assays. By adding drugs to cultures of differentiated cells such as kidney cells, liver cells, brain cells, heart **smooth muscle**, chondrocytes, pancreatic cells, neuronal cells, blood cells etc, it is possible to avoid the use of animals in preclinical testing...

this mention does not teach or suggest how one of ordinary art could provide one or more of Applicants' claimed inventions as a whole. Applicants also submit that Benvenisty's use of Activin A, for example as indicated in the Office Action and appearing in paragraph 0070,

[0070] Since growth factor receptors were expressed in 5 day old EBs, we could examine the effects of the corresponding ligands on differentiation. After several days of culture on plastic and continuous exposure to growth factors, the cells acquired different morphologies (FIG. 1-B). Without growth factors, cells

spontaneously differentiated into many different types of colonies, whereas the addition of growth factors produced more mature cell morphologies such as syncytial myocytes and neuronal cells. Compared to control DE cells, the growth factor treated cultures were more homogenous and up to half of the culture contained one or two cell types. For example, large populations of small cells with pronounced nuclei were found in cultures treated with HGF (FIG. 1-B-I), **muscle** like syncytiums in the Activin-A treated cells (FIG. 1-B-III), neuronal like cells in the RA treated culture (FIG. 1-B-IV), fibroblast like cells in the cultures treated with bFGF (FIG. 1-B-V), and large round cells in cultures treated with BMP-4 (FIG. 1-B-VI). These varied cell morphologies demonstrate that specific programs are initiated as a result of growth factor treatment.

does not teach or suggest that alone or in combination one of ordinary skill in the art could provide a tissue engineering construct comprising smooth muscle cells having a three dimensional vascular network. As set forth in Applicants' claim 1 or 23 because, as noted by Applicants (see, e.g., page 32, lines 20-24) that differentiation on scaffolds is different than that provided from chemical factors alone. As a result, given the unpredictable nature of the art, one of ordinary skill in the art would not have reasonably expected to successfully combine the teachings of Levenberg and Benvenisty to produce either Applicants claim 1 or 23. Accordingly, Applicants respectfully submit that claims 1 and 23, and claims 2-5, 7-11, 13-19, 22, 24-25, 27-34, 36-44, 47-50, and 71-74, that ultimately depend from one 1 and 23, are novel and non-obvious over Levenberg and Benvenisty either alone or in proper combination.

Rejections under 35 U.S.C. §103 based on Levenberg, Benvenisty & Kojima

As set forth above, Levenberg and Benvenisty, either alone or in proper combination, fail to teach tissue engineering constructs comprising smooth muscle cells having a three dimensional vascular network and methods for making same as set forth in Applicants' claims. Applicants further submit that Kojima does not cure this deficiency in Levenberg and Benvenisty.

Specifically, Kojima does not address a tissue engineering construct comprising embryonic stem cells and at least one growth factor selected to promote differentiation of the

stem cells into smooth muscle cells having a three dimensional vascular network as set forth in Applicants' claim 1 or methods for producing a tissue engineering construct by, inter alia, exposing a population of embryonic stem cells to at least one agent selected to promote differentiation of the stem cells into smooth muscle cells having a three dimensional vascular network. Rather, Kojima is focused solely on the effects of chemical factors on mature, fully differentiated cells, and in particular on the nuclear labeling of such cells. As a result, Applicants respectfully submit that Kojima, Levenberg and Benvenisty, either alone or in proper combination, do not teach each and every element of either of Applicants independent claims, and thus Applicants claims are novel and non-obvious over the cited references.

### **CONCLUSION**

Although Applicants currently traverse the rejections of the claims based on Levenberg and Benvenisty, Applicants do not acquiesce in the view that Levenberg and Benvenisty are properly prior art to the present inventions. Applicants are currently investigating whether the inventions of the present application were invented before the publication of Levenberg or Benvenisty, or invented by another in Levenberg.

In view of the above, it is believed that all presently pending claims are in condition for allowance, and it is respectfully requested that the claims be allowed. If the Examiner feels that a telephone call would expedite the prosecution of this case, the Examiner is invited to call the undersigned at (617) 248-5016.

Respectfully submitted,

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